REMARKS

Claims 24-33 are pending. Applicants submit the following remarks in response to the enablement rejection issued in the Final Office Action mailed 26 November 2001. All other rejections and objections have been withdrawn in response to Applicants' response and amendment, filed 14 August 2001. Consideration of the following remarks is respectfully requested.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 24-33 stand rejected under 35 U.S.C. §112, first paragraph, as lacking enablement. Applicants respectfully traverse.

The pending claims are directed to nucleic acids encoding Mkinase proteins, vectors and host cells comprising the same, and uses thereof. The claimed nucleic acid compositions are defined in terms of their sequence identity (comprising or encoding sequences having at least about 95% identity to listed sequences) and the binding properties of the proteins they encode (binding to Traf4).

The Office Action expresses that one of skill in the art would not know how to use the claimed nucleic acid compositions. In particular, the Office Action states that one would not be able to use the claimed compositions without further experimentation to determine what the function of Mkinase is.

However, having considered the teaching of the specification, as well as that of the declaration of Xiang Xu filed under §1.32, the Office Action concedes at page 3 that "one of skill in the art might conclude that Mkinase is somehow involved in the cell cycle, ..."

Applicants submit that knowing Mkinase is somehow involved in the cell cycle is sufficient to enable one of skill in the art to make and use the same to screen for modulators of the cell cycle. Moreover, Applicants submit that screening assays that make use of Mkinase and are designed to identify modulators of the cell cycle have substantial, real world utility. Both the specification and the Xiang Xu declaration teach that Mkinase is a modulator (e.g., inhibitor, or enhancer) of the cell cycle, as acknowledged in the Office Action by the admission "somehow involved in the cell cycle". Further, the importance of the cell cycle to disease is well known. Accordingly, the screening assays have a real world utility which does not require further research to define. In support, Applicants respectfully direct the Examiner to the M.P.E.P. §2107.01, which states, "...an assay method for identifying compounds that themselves have a "substantial" utility define a "real world" context of use."

In further regard to the teachings of the Xiang Xu declaration, Applicants respectfully direct the Examiner to the Revised Utility Guidelines, Federal Register, 66(4), pp. 1097-1099, January 5, 2001, which state:

> Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement.
>
> Similarly, Office personnel must accept an opinion from a qualified expert that is based upon relevant facts whose accuracy is not being questioned; it is improper to disregard the opinion solely because of a disagreement over the significance or meaning of the facts offered.

The Office Action provides no evidence to refute the teachings of the Xiang Xu declaration, or to suggest that the asserted function of Mkinase is not credible, or that the

claimed nucleic acids would be inoperative. Absent such evidence, Applicants submit that one of skill in the art would accept the asserted functions of Mkinase as credible, and be able to make and use the claimed invention for a substantial, real world utility.

How to Use

The Office Action states at page 4 that the specification fails to teach whether Mkinase arrests or stimulates cell division, suggesting that this would keep one of skill in the art from being able to use the invention.

However, at page 31, the specification describes cell-based assays designed to screen for agents capable of modulating the activity of Mkinase. The specification states:

> In a preferred embodiment, the invention provides methods for screening for bioactive agents capable of modulating the activity of an cell cycle protein. The methods comprise adding a candidate bioactive agent, as defined above, to a cell comprising cell cycle proteins. Preferred cell types include almost any cell. The cells contain a recombinant nucleic acid that encodes an cell cycle protein. In a preferred embodiment, a library of candidate agents are tested on a plurality of cells.

Applicants submit that one of skill in the art, knowing that Mkinase was a modulator of the cell cycle, would look for changes in the cell cycle to reflect changes in Mkinase activity. Moreover, at page 31, the specification states that both antagonists and agonists of cell cycle protein activity are desired, meaning screens that identify inhibitors and screens that identify enhancers of proliferation are desirable. Accordingly, screens that use Mkinase as a modulator of the cell cycle, whether as an enhancer or inhibitor, are desirable.

Finally, the nature of the cell cycle regulation assays set forth in the specification is such that the way in which Mkinase modulates cell cycle regulation, i.e., increasing or

decreasing cell proliferation, is not critical to the performance of the assay. At page 32, line 15, the specification describes methods for screening for alterations in cell cycle regulation. Importantly, what is measured is a change in the cell cycle, i.e., a proliferating cell arrests, or an arrested cell starts to proliferate. Further, at page 32, line 26, the specification states that the measurements may be made in the presence and absence of a candidate agent, where all other conditions are the same.

Applicants submit that such methods do not require the use of an enhancer, specifically, or an inhibitor, specifically, of the cell cycle. Rather, a modulator of the cell cycle is required (either enhancer or inhibitor) against which agents may be screened for cell cycle activity. Further, as stated in the specification, both agonists and antagonists capable of increasing and decreasing cell proliferation are desired.

Accordingly, Applicants submit that one of skill in the art would be able to make and use the claimed nucleic acid compositions, for example, to screen for modulators of the cell cycle.

CONCLUSION

Applicants submit that the application is in form for allowance and early notification of such is requested. If there remain issues that the Examiner believes may be resolved by telephone, he is respectfully requested to contact the undersigned at (415) 781-1989.

Respectfully submitted,

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